

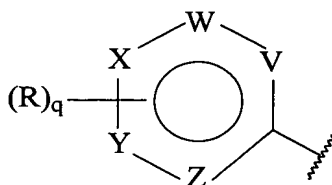
WHAT IS CLAIMED IS:

1. A method of modulating the activity of excitatory amino acid receptors, said method comprising:

contacting said receptors with at least one compound having the structure

5 **A — L — B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, in an amount sufficient to modulate the activity of said excitatory amino acid receptor, wherein :

A is a 5-, 6- or 7-membered ring having the structure:



10 wherein at least one of **V, W, X, Y and Z** is (CR)_p, wherein p is 0, 1 or 2;
at least one of **V, W, X, Y and Z** is O, N or S;
the remainder of **V, W, X, Y and Z** are each independently O, N or S; and
each **R** is independently halogen, substituted or unsubstituted hydrocarbyl,
substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate,
15 carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide,
wherein q is 0, 1, 2 or 3;

L is substituted or unsubstituted alkenylene, alkynylene, or azo; and

B is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted
cyclohydrocarbyl, substituted or unsubstituted heterocycle, optionally containing one
20 or more double bonds, or substituted or unsubstituted aryl;

provided, that the following compounds are excluded: the compounds wherein **A** is a
6-membered ring wherein:

V, W, X and Y are (CR)_p, wherein p is 1;

Z is N;

25 **R** at the **V** position is hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl,
amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl,
unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower
alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-

lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower alkoxy or esterified carboxy-lower-alkoxy; R at the W position is hydrogen; R at the X position is hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy; and R at the Y position is hydrogen, lower alkyl, hydroxy-lower alkyl, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy;

L is substituted or unsubstituted alkenylene, alkynylene or azo, and

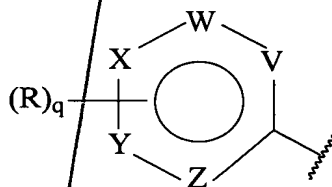
B is substituted or unsubstituted aryl or heterocycle having two or more double bonds, wherein substituents are independently lower alkyl, lower alkenyl, lower alkynyl, phenyl, phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, phenoxy, phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, nitro, amino, acylamino, N-acyl-N-lower alkylamino, halo and halo-lower alkyl, wherein phenyl, phenyl-lower alkynyl, phenoxy, and phenyl-lower alkoxy may bear further substituents.

2. A method according to claim 1, wherein said excitatory amino acid receptor is a metabotropic glutamate receptor.

3. A method according to claim 2, wherein said metabotropic glutamate receptor is a Group 1 metabotropic glutamate receptor.

4. A method for treating disease conditions, said method comprising:
administering to a patient having a disease condition a therapeutically
effective amount of at least one compound having the structure **A — L — B** or enantiomers,
diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically
5 acceptable salts thereof, wherein :

A is a 5-, 6- or 7-membered ring having the structure:



wherein at least one of **V, W, X, Y and Z** is $(CR)_p$, wherein **p** is 0, 1 or 2;
at least one of **V, W, X, Y and Z** is O, N or S;
the remainder of **V, W, X, Y and Z** are each independently O, N or S; and
each **R** is independently halogen, substituted or unsubstituted hydrocarbyl,
substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate,
carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide,
wherein **q** is 0, 1, 2 or 3;

L is substituted or unsubstituted alkenylene, alkynylene, or azo; and
B is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted
cyclohydrocarbyl, substituted or unsubstituted heterocycle, optionally containing one
or more double bonds, or substituted or unsubstituted aryl;
provided, that the following compounds are excluded: the compounds wherein **A** is a
6-membered ring wherein:

V, W, X and Y are $(CR)_p$, wherein **p** is 1;
Z is N;
R at the **V** position is hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl,
amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl,
unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower
alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-
lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-

yl-substitued lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower alkoxy or esterified carboxy-lower-alkoxy; R at the W position is hydrogen; R at the X position is hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy; and R at the Y position is hydrogen, lower alkyl, hydroxy-lower alkyl, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy;

L is substituted or unsubstituted alkenylene, alkynylene or azo, and

B is substituted or unsubstituted aryl or heterocycle having two or more double bonds, wherein substituents are independently lower alkyl, lower alkenyl, lower alkynyl, phenyl, phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylendioxy, lower alkanoyloxy, phenoxy, phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, nitro, amino, acylamino, N-acyl-N-lower alkylamino, halo and halo-lower alkyl, wherein phenyl, phenyl-lower alkynyl, phenoxy, and phenyl-lower alkoxy may bear further substituents.

5. A method according to claim 4, wherein said disease condition is cerebral ischemia, chronic neurodegeneration, psychiatric disorders, schizophrenia, mood disorders, emotion disorders, disorders of extrapyramidal motor function, obesity, disorders of respiration, motor control and function, attention deficit disorders, concentration disorders, pain disorders, neurodegenerative disorders, epilepsy, convulsive disorders, eating disorders, sleep disorders, sexual disorders, circadian disorders, drug withdrawal, drug addiction, compulsive disorders, anxiety, panic disorders, depressive disorders, skin disorders, retinal ischemia, retinal degeneration, glaucoma, disorders associated with organ transplantation, asthma, ischemia or astrocytomas.

6. A method according to claim 5, wherein said mood disorder is anxiety, depression, psychosis, drug withdrawal, tobacco withdrawal, memory loss, cognitive impairment, dementia, or Alzheimer's disease.

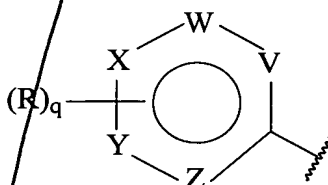
7. A method according to claim 5, wherein said extrapyramidal motor function is Parkinson's disease, progressive supramuscular palsy, Huntington's disease, Gilles de la Tourette syndrome, or tardive dyskinesia.

8. A method according to claim 5, wherein said pain disorder is neuropathic pain, chronic pain, acute pain, painful diabetic neuropathy, post-herpetic neuralgia, cancer-associated pain, pain associated with chemotherapy, pain associated with spinal cord injury, pain associated with multiple sclerosis, causalgia and reflex sympathetic dystrophy, phantom pain, post-stroke (central) pain, pain associated with HIV or AIDS, trigeminal neuralgia, lower back pain, myofacial disorders, migraine, osteoarthritic pain, postoperative pain, dental pain, post-burn pain, pain associated with systemic lupus, entrapment neuropathies, painful polyneuropathies, ocular pain, pain associated with inflammation or pain due to tissue injury.

9. A method for preventing disease conditions in a subject at risk thereof, said method comprising:

administering to said subject a therapeutically effective amount of at least one compound having structure **A — L — B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, or pharmaceutically acceptable salts thereof, wherein :

A is a 5-, 6- or 7-membered ring having the structure:



wherein at least one of **V, W, X, Y and Z** is $(CR)_p$, wherein p is 0, 1 or 2;

at least one of **V, W, X, Y and Z** is O, N or S;

the remainder of **V, W, X, Y and Z** are each independently O, N or S; and

each **R** is independently halogen, substituted or unsubstituted hydrocarbyl, substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide, wherein q is 0, 1, 2 or 3;

L is substituted or unsubstituted alkenylene, alkynylene, or azo; and

B is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted cyclohydrocarbyl, substituted or unsubstituted heterocycle, optionally containing one or more double bonds, or substituted or unsubstituted aryl;

provided, that the following compounds are excluded: the compounds wherein **A** is a 6-membered ring wherein:

V, W, X and Y are $(CR)_p$, wherein p is 1;

Z is N;

R at the **V** position is hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy,

carboxy-lower alkoxy or esterified carboxy-lower-alkoxy; R at the W position is hydrogen; R at the X position is hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy; and R at the Y position is hydrogen, lower alkyl, hydroxy-lower alkyl, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy;

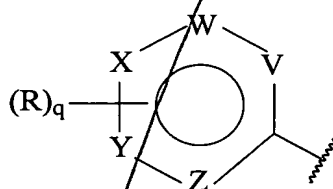
L is substituted or unsubstituted alkenylene, alkynylene or azo, and

B is substituted or unsubstituted aryl or heterocycle having two or more double bonds, wherein substituents are independently lower alkyl, lower alkenyl, lower alkynyl, phenyl, phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, phenoxy, phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, nitro, amino, acylamino, N-acyl-N-lower alkylamino, halo and halo-lower alkyl, wherein phenyl, phenyl-lower alkynyl, phenoxy, and phenyl-lower alkoxy may bear further substituents.

10. A method according to claim 9, wherein said disease is a disease of the pulmonary system, a disease of the nervous system, a disease of the cardiovascular system, a disease of the gastrointestinal system, a disease of the endocrine system, a disease of the exocrine system, a disease of the skin, cancer or a disease of the ophthalmic system.

11. A pharmaceutically acceptable salt form of a compound, said compound having the formula **A — L — B** or enantiomers, diastereomeric isomers or mixtures of any two or more thereof, wherein :

A is a 5-, 6- or 7-membered ring having the structure:



wherein at least one of **V, W, X, Y and Z** is $(CR)_p$, wherein p is 0, 1 or 2;

at least one of **V, W, X, Y and Z** is O, N or S;

the remainder of **V, W, X, Y and Z** are each independently O, N or S; and

each **R** is independently halogen, substituted or unsubstituted hydrocarbyl,

substituted or unsubstituted aryl, heterocycle, mercapto, nitro, carboxyl, carbamate, carboxamide, hydroxy, ester, cyano, amine, amide, amidine, amido, sulfonyl or sulfonamide, wherein q is 0, 1, 2 or 3;

L is substituted or unsubstituted alkenylene, alkynylene, or azo; and

B is substituted or unsubstituted hydrocarbyl, substituted or unsubstituted cyclohydrocarbyl, substituted or unsubstituted heterocycle, optionally containing one or more double bonds, or substituted or unsubstituted aryl; and

the salt is acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, heptanoate, hexanoate, 2-hydroxyethanesulfonate, lactate, malate, maleate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, tartrate, toluenesulfonate, undecanoate, sulfate, bisulfate, hemisulfate, hydrochloride, hydrobromide, hydroiodide, an ammonium salt, an alkali metal salt, an alkaline earth metal salt, a dicyclohexylamine salt, *N*-methyl-D-glucamine, phenylethylamine, or an amino acid salt;

provided, that the following compounds are excluded: the compounds wherein **A** is a 6-membered ring wherein:

V, W, X and Y are $(CR)_p$, wherein p is 1;

Z is N;

Sub

R at the V position is hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower alkoxy or esterified carboxy-lower-alkoxy; R at the W position is hydrogen; R at the X position is hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy; and R at the Y position is hydrogen, lower alkyl, hydroxy-lower alkyl, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower alkyl-N-phenylcarbonyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy;

L is substituted or unsubstituted alkenylene, alkynylene or azo, and

B is substituted or unsubstituted aryl or heterocycle having two or more double bonds, wherein substituents are independently lower alkyl, lower alkenyl, lower alkynyl, phenyl, phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, phenoxy, phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, nitro, amino, acylamino, N-acyl-N-lower alkylamino, halo and halo-lower alkyl, wherein phenyl, phenyl-lower alkynyl, phenoxy, and phenyl-lower alkoxy may bear further substituents.

12/ The pharmaceutically acceptable salt form of the compound, wherein the salt is a toluene/sulfonic acid salt.